EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	6	(harris brimble).in. and neuroprotect$.ti.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/07/28 11:33

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=> b reg
FILE 'REGISTRY' ENTERED AT 10:33:43 ON 28 JUL 2007
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provided by InfoChem.

STRUCTURE FILE UPDATES:   27 JUL 2007  HIGHEST RN 943585-98-6
DICTIONARY FILE UPDATES:  27 JUL 2007  HIGHEST RN 943585-98-6

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d que sta l16
L1              STR
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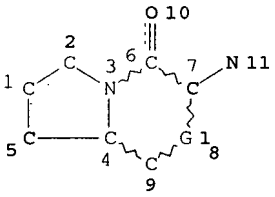


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L16         1389 SEA FILE=REGISTRY SSS FUL L1

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SEARCH TIME: 00.00.01


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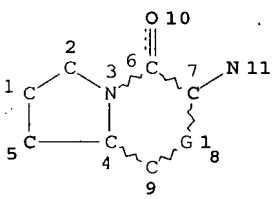


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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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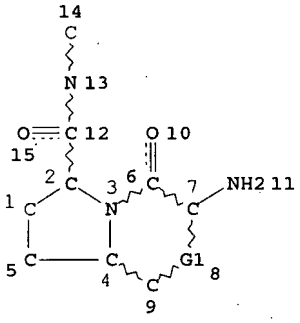

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.01

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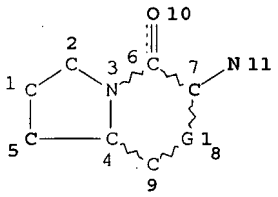

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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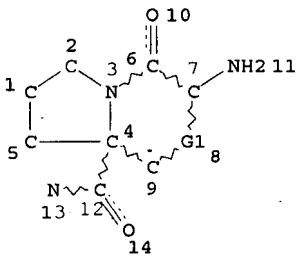


REP G1=(0-3) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L34 5 SEA FILE=REGISTRY SUB=L16 SSS FUL L32

100.0% PROCESSED 136 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

=> b hcap
FILE 'HCAPLUS' ENTERED AT 10:33:56 ON 28 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

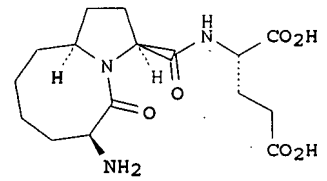
FILE COVERS 1907 - 28 Jul 2007 VOL 147 ISS 6
FILE LAST UPDATED: 27 Jul 2007 (20070727/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitstr l11 tot

L11 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:657613 HCAPLUS
DN 145:293325
TI Synthesis of macrocyclic analogues of the neuroprotective agent glycyl-L-prolyl-L-glutamic acid (GPE)
AU Harris, Paul W. R.; Brimble, Margaret A.
CS Department of Chemistry, University of Auckland, Auckland, N. Z.
SO Organic & Biomolecular Chemistry (2006), 4(14), 2696-2709
CODEN: OBCRAK; ISSN: 1477-0520
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 145:293325
GI



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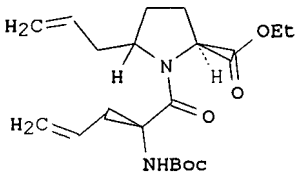


II

AB Seven macrocyclic analogs, e.g., I•TFA, of the neuroprotective tripeptide glycyl-L-prolyl-L-glutamic acid (GPE) were prepared via Grubbs ring closing metathesis of an appropriate diene precursor, which was obtained from allyl-substituted amino acid building blocks, e.g., II (Boc = tert-butoxycarbonyl). Two of the macrocycles mimic the cis conformer of GPE, whereas the others, including I•TFA, mimic the trans conformer of GPE.

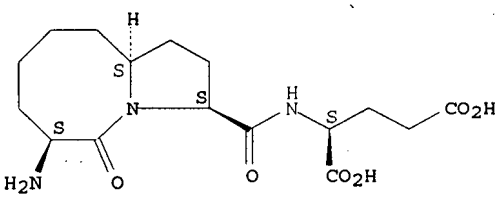
IT **765313-71-1P 765313-87-9P 908568-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of macrocyclic analogs of neuroprotective agent glycyl-L-prolyl-L-glutamic acid via Grubbs ring closing metathesis)

RN 765313-71-1 HCAPLUS
CN L-Glutamic acid, N-[[(3S,6S,10aS)-6-aminodecahydro-5-oxopyrrolo[1,2-a]azocin-3-yl]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

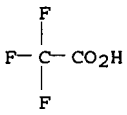
CRN 765313-70-0
CMF C16 H25 N3 O6

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

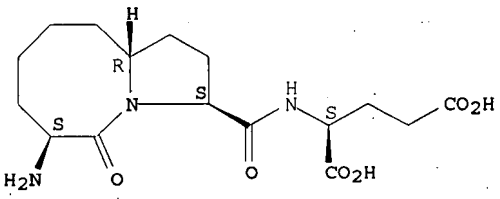


RN 765313-87-9 HCAPLUS
CN L-Glutamic acid, N-[[(3S,6S,10aR)-6-aminodecahydro-5-oxopyrrolo[1,2-a]azocin-3-yl]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 765313-86-8
CMF C16 H25 N3 O6

Absolute stereochemistry.



CM 2

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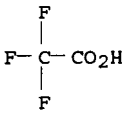
CMF C2 H F3 O2

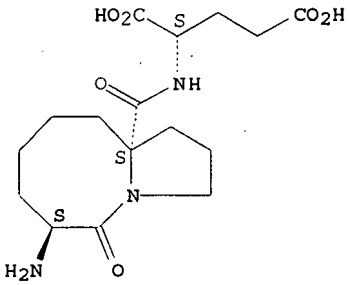


RN 908568-57-0 HCAPLUS
CN L-Glutamic acid, N-[[(6S,10aS)-6-aminooctahydro-5-oxopyrrolo[1,2-a]azocin-10a(1H)-yl]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 908568-56-9
CMF C16 H25 N3 O6

Absolute stereochemistry. Rotation (-).



CM 2

CRN 76-05-1
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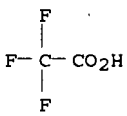

RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:817638 HCAPLUS
DN 141:314630
TI Preparation of neuroprotective macrocyclic compounds
IN Harris, Paul W. R.; Brimble, Margaret Anne

PA Neuronz Limited, N. Z.; Neuronz Biosciences, Inc.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO2004084809	A2	20041007	2004WO-US08108	20040316
WO2004084809	A3	20050630		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP---1648873	A2	20060426	2004EP-0757761	20040316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP2006523213	T	20061012	2006JP-0507261	20040316
US2006217295	A1	20060928	2005US-0549951	20050920
PRAI 2003US-456136P	P	20030320		
2003US-505119P	P	20030923		
2004WO-US08108	W	20040316		

OS MARPAT 141:314630
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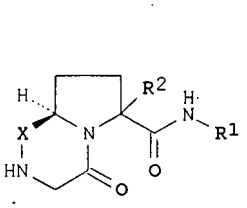

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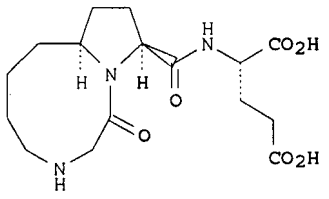


II

AB The invention relates to macrocyclic peptidomimetics, e.g., I [R1, R2 are H, OR', SR', NR'2, NO2, CN, C(O)R', C(O)OR', C(O)NR'2, C(NR')NR'2, trihalomethyl, halo, (un)substituted alkyl, heteroalkyl, alkenyl, alkynyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl, where R' is H, alkyl, heteroalkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl; X is C0-C4 alkyl or alkenyl], or their pharmaceutically-acceptable salts that are neuroprotective and have utility as therapeutic agents for the treatment of diseases, injuries and other conditions characterized by neuronal degeneration and/or death. Thus, macrocyclic compound II TFA salt was prepared via cyclization of cis-N-[allyl(benzyloxycarbonyl)glycyl]-5-allylproline tert-Bu ester and assayed for biol. activity (neuronal survival in animals following excitotoxic oxidative stress and neuroprotective effects in a global model of brain ischemia).

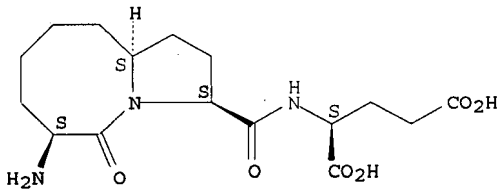
IT **765313-71-1P 765313-87-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of neuroprotective macrocyclic compds.)

RN 765313-71-1 HCAPLUS
CN L-Glutamic acid, N-[[(3S,6S,10aS)-6-aminodecahydro-5-oxopyrrolo[1,2-a]azocin-3-yl]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 765313-70-0
CMF C16 H25 N3 O6

Absolute stereochemistry.



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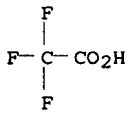
CRN 76-05-1
CMF C2 H F3 O2

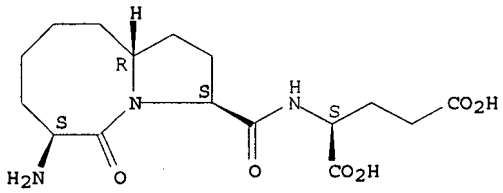


RN 765313-87-9 HCAPLUS
CN L-Glutamic acid, N-[[(3S,6S,10aR)-6-aminodecahydro-5-oxopyrrolo[1,2-a]azocin-3-yl]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 765313-86-8
CMF C16 H25 N3 O6

Absolute stereochemistry.



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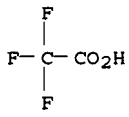

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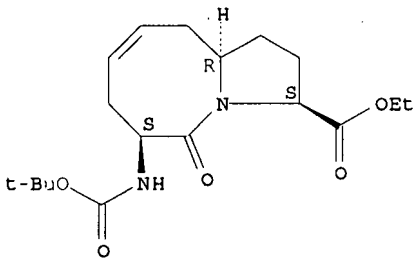
L40 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1108672 HCAPLUS
DN 146:81752
TI Synthesis and evaluation of novel 8,5-fused bicyclic peptidomimetic compounds as interleukin-1β converting enzyme (ICE) inhibitors
AU Soper, David L.; Sheville, Justin X.; O'Neil, Steven V.; Wang, Yili; Laufersweiler, Michael C.; Oppong, Kofi A.; Wos, John A.; Ellis, Christopher D.; Baize, Mark W.; Chen, Jack J.; Fancher, Amy N.; Lu, Wei; Suchanek, Maureen K.; Wang, Richard L.; Schwecke, William P.; Cruze, Charles A.; Buchalova, Maria; Belkin, Marina; Wireko, Fred; Ritter, Amanda; De, Biswanath; Wang, Difei; Demuth, Thomas P.

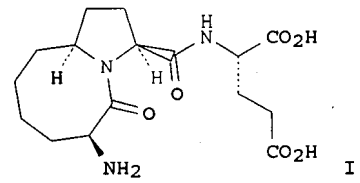
CS Procter & Gamble Pharmaceuticals, Inc., Mason, OH, 45040, USA
SO Bioorganic & Medicinal Chemistry (2006), 14(23), 7880-7892
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 146:81752
AB An 8,5-fused bicyclic peptidomimetic ring system generated by a stereoselective ring metathesis reaction was elaborated into potent inhibitors of interleukin-1β converting enzyme (ICE, caspase-1). Multiple compds. were found that exhibited ICE IC50 values <10 nM and were selective over caspase-3 and caspase-8. These active analogs generally possessed good activity (IC50 values <100 nM) in a whole cell assay measuring IL-1β production Pharmacokinetic anal. of the Et acetal prodrug form of a selected active lead revealed a compound with a reasonable plasma half-life (1.1 h) and good oral bioavailability (30%).
IT **549521-78-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and evaluation of peptidomimetic octahydropyrroloazocinecarboxamides as interleukin-1β converting enzyme inhibitors)
IT **549521-78-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and evaluation of peptidomimetic octahydropyrroloazocinecarboxamides as interleukin-1β converting enzyme inhibitors)
RN 549521-78-0 HCAPLUS
CN Pyrrolo[1,2-a]azocine-3-carboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]-1,2,3,5,6,7,10,10a-octahydro-5-oxo-, ethyl ester, (3S,6S,10aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:657613 HCAPLUS
DN 145:293325
TI Synthesis of macrocyclic analogues of the neuroprotective agent glycyl-L-prolyl-L-glutamic acid (GPE)
AU **Harris, Paul W. R.**; **Brimble, Margaret A.**
CS Department of Chemistry, University of Auckland, Auckland, N. Z.
SO Organic & Biomolecular Chemistry (2006), 4(14), 2696-2709
CODEN: OBCRAK; ISSN: 1477-0520
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 145:293325
GI



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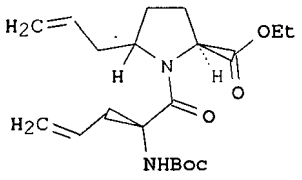


II

AB Seven macrocyclic analogs, e.g., I•TFA, of the neuroprotective tripeptide glycyl-L-prolyl-L-glutamic acid (GPE) were prepared via Grubbs ring closing metathesis of an appropriate diene precursor, which was obtained from allyl-substituted amino acid building blocks, e.g., II (Boc = tert-butoxycarbonyl). Two of the macrocycles mimic the cis conformer of GPE, whereas the others, including I•TFA, mimic the trans conformer of GPE.

IT **549521-78-0P 549521-80-4P 549521-81-5P**
765313-56-2P 765313-68-6P 765313-69-7P
765313-84-6P 765313-85-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of macrocyclic analogs of neuroprotective agent glycyl-L-prolyl-L-glutamic acid via Grubbs ring closing metathesis)

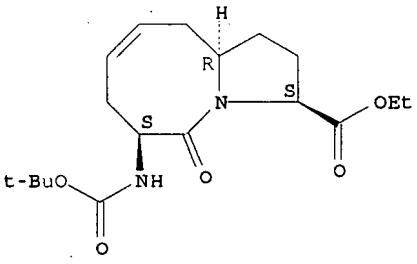
IT **765313-71-1P 765313-87-9P 908568-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of macrocyclic analogs of neuroprotective agent glycyl-L-prolyl-L-glutamic acid via Grubbs ring closing metathesis)

IT **549521-78-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of macrocyclic analogs of neuroprotective agent glycyl-L-prolyl-L-glutamic acid via Grubbs ring closing metathesis)

RN 549521-78-0 HCAPLUS

CN Pyrrolo[1,2-a]azocine-3-carboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]-1,2,3,5,6,7,10,10a-octahydro-5-oxo-, ethyl ester, (3S,6S,10aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



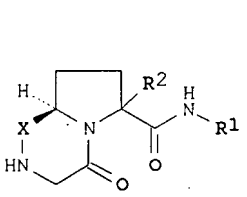
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:817638 HCAPLUS
DN 141:314630
TI Preparation of neuroprotective macrocyclic compounds
IN **Harris, Paul W. R.**; **Brimble, Margaret Anne**
PA Neuronz Limited, N. Z.; Neuronz Biosciences, Inc.
SO PCT Int. Appl., 106 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2004084809	A2	20041007	2004WO-US08108	20040316 <--
	WO2004084809	A3	20050630		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP---1648873	A2	20060426	2004EP-0757761	20040316 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	JP2006523213	T	20061012	2006JP-0507261	20040316 <--
	US2006217295	A1	20060928	2005US-0549951	20050920 <--
PRAI	2003US-456136P	P	20030320 <--		
	2003US-505119P	P	20030923 <--		
	2004WO-US08108	W	20040316 <--		

OS MARPAT 141:314630
GI



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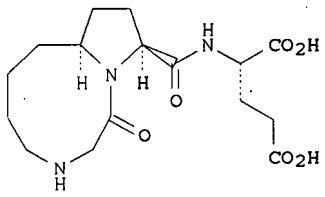


II

AB The invention relates to macrocyclic peptidomimetics, e.g., I [R1, R2 are H, OR', SR', NR'2, NO2, CN, C(O)R', C(O)OR', C(O)NR'2, C(NR')NR'2, trihalomethyl, halo, (un)substituted alkyl, heteroalkyl, alkenyl, alkynyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl, where R' is H, alkyl, heteroalkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl; X is C0-C4 alkyl or alkenyl], or their pharmaceutically-acceptable salts that are neuroprotective and have utility as therapeutic agents for the treatment of diseases, injuries and other conditions characterized by neuronal degeneration and/or death. Thus, macrocyclic compound II TFA salt was prepared via cyclization of cis-N-[allyl(benzyloxycarbonyl)glycyl]-5-allylproline tert-Bu ester and assayed for biol. activity (neuronal survival in animals following excitotoxic oxidative stress and neuroprotective effects in a global model of brain ischemia).

IT **765313-58-4P 765313-71-1P 765313-87-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of neuroprotective macrocyclic compds.)

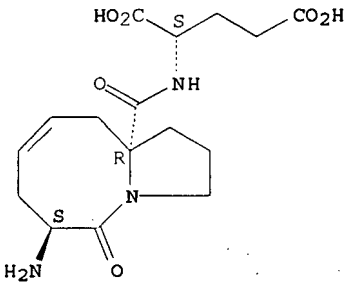
IT **765313-58-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of neuroprotective macrocyclic compds.)

RN 765313-58-4 HCAPLUS
CN L-Glutamic acid, N-[[(6S,10aR)-6-amino-2,3,5,6,7,10-hexahydro-5-oxopyrrolo[1,2-a]azocin-10a(1H)-yl]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

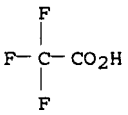
CRN 765313-57-3
CMF C16 H23 N3 O6

Absolute stereochemistry.

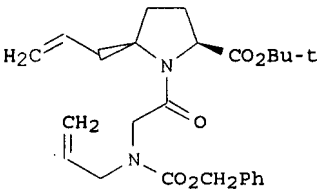


CM 2

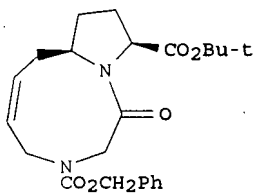
CRN 76-05-1
CMF C2 H F3 O2



L40 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:326583 HCAPLUS
DN 139:69511
TI Synthesis of Cyclic Proline-Containing Peptides via Ring-Closing Metathesis
AU Harris, Paul W. R.; Brimble, Margaret A.; Gluckman, Peter D.
CS NeuronZ Medicinal Chemistry Group, Department of Chemistry, University of Auckland, Auckland, N. Z.
SO Organic Letters (2003), 5(11), 1847-1850
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
OS CASREACT 139:69511
GI



I



II

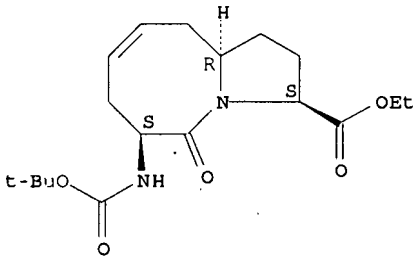
AB Several dienes embedded in di- and tripeptides which incorporate proline have been prepared and subjected to ring-closing metathesis. Bicyclic peptides of well-defined amide geometry and of varying ring sizes were prepared For example, allylprolinate I underwent ring-closing metathesis in presence of Grubbs catalyst in CH2Cl2 to give cyclic peptide II in 46% yield after 48 h. Several limitations of the cyclization step were revealed.
IT **549521-78-0P 549521-80-4P 549521-81-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of cyclic proline peptides via ring-closing metathesis reaction)

IT **549521-78-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of cyclic proline peptides via ring-closing metathesis reaction)

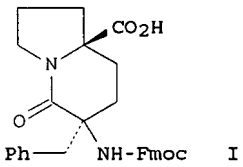
RN 549521-78-0 HCAPLUS
CN Pyrrolo[1,2-a]azocine-3-carboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]-1,2,3,5,6,7,10,10a-octahydro-5-oxo-, ethyl ester, (3S,6S,10aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:858286 HCAPLUS
DN 124:56673
TI Synthesis of a type-VIβ-turn peptide mimetic and its incorporation into a high-affinity somatostatin receptor ligand
AU Gramberg, Dieter; Weber, Christoph; Beeli, Reto; Inglis, Janice; Bruns, Christian; Robinson, John A.
CS Institute Organic Chemistry, University Zuerich, Zurich, CH-8057, Switz.
SO Helvetica Chimica Acta (1995), 78(6), 1588-606
CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta
DT Journal
LA English
OS CASREACT 124:56673
GI

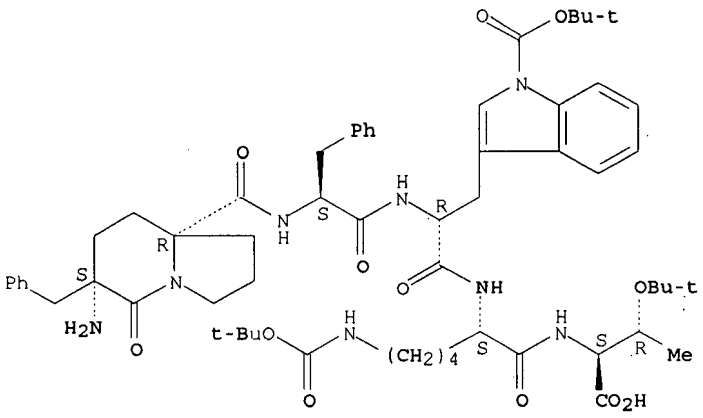


I

AB The synthesis of a cis-Phe-Pro dipeptide mimetic is described, which adopts a type-VIβ-turn conformation. The α-positions of Phe and Pro are joined by a CH2CH2 bridge, thereby forming a fused bicyclic system, and fixing a geometry similar to that seen in cis-Phe-Pro units in protein crystal structures. The dipeptide mimetic I was synthesized in optically pure form starting from (R)-α-allylproline, with a free carboxylic acid and an Fmoc-protected N-terminus, thereby allowing its incorporation into linear and cyclic peptides using standard solid-phase methods. The mimetic I was incorporated into the cyclic somatostatin analog cyclo(-Phe=Pro-Phe-D-Trp-Lys-Thr-), where Phe=Pro represents the mimetic. This analog shows a high affinity for somatostatin receptors. Based on NMR studies in aqueous solution, likely low-energy conformations for this analog were deduced using restrained dynamic simulated annealing. The conformations found, which include a distorted type-II' turn at D-Trp-Lys, are similar to low-energy conformations for cyclo(-Phe-Pro-Phe-D-Trp-Lys-Thr-), and to those in crystal structures of octreotide.

IT **172039-57-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of a type-VIβ-turn peptide mimetic and a high-affinity somatostatin receptor ligand containing it)
IT **172039-57-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of a type-VIβ-turn peptide mimetic and a high-affinity somatostatin receptor ligand containing it)
RN 172039-57-5 HCAPLUS
CN L-Threonine, N-[N2-[N-[N-[[6-aminohexahydro-5-oxo-6-(phenylmethyl)-8a(1H)-indolizinyl]carbonyl]-L-phenylalanyl]-1-[(1,1-dimethylethoxy)carbonyl]-D-tryptophyl]-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl]-O-(1,1-dimethylethyl)-, (6S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

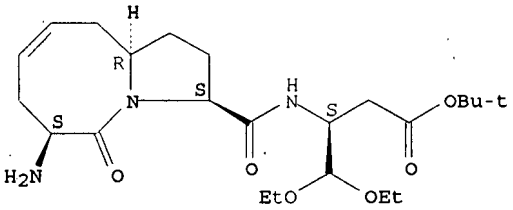


=> d bib abs hitstr l30 tot

L30 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1108672 HCAPLUS
DN 146:81752
TI Synthesis and evaluation of novel 8,5-fused bicyclic peptidomimetic compounds as interleukin-1β converting enzyme' (ICE) inhibitors
AU Soper, David L.; Sheville, Justin X.; O'Neil, Steven V.; Wang, Yili; Laufersweiler, Michael C.; Oppong, Kofi A.; Wos, John A.; Ellis, Christopher D.; Baize, Mark W.; Chen, Jack J.; Fancher, Amy N.; Lu, Wei; Suchanek, Maureen K.; Wang, Richard L.; Schwecke, William P.; Cruze, Charles A.; Buchalova, Maria; Belkin, Marina; Wireko, Fred; Ritter, Amanda; De, Biswanath; Wang, Difei; Demuth, Thomas P.
CS Procter & Gamble Pharmaceuticals, Inc., Mason, OH, 45040, USA
SO Bioorganic & Medicinal Chemistry (2006), 14(23), 7880-7892
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 146:81752
AB An 8,5-fused bicyclic peptidomimetic ring system generated by a stereoselective ring metathesis reaction was elaborated into potent inhibitors of interleukin-1β converting enzyme (ICE, caspase-1). Multiple compds. were found that exhibited ICE IC50 values <10 nM and were selective over caspase-3 and caspase-8. These active analogs generally possessed good activity (IC50 values <100 nM) in a whole cell assay measuring IL-1β production Pharmacokinetic anal. of the Et acetal prodrug form of a selected active lead revealed a compound with a reasonable plasma half-life (1.1 h) and good oral bioavailability (30%).
IT **917244-20-3DP**, amides
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and evaluation of peptidomimetic octahydropyrroloazocinecarboxamides as interleukin-1β converting enzyme inhibitors)
RN 917244-20-3 HCAPLUS
CN Butanoic acid, 3-[[[(3S,6S,10aR)-6-amino-1,2,3,5,6,7,10,10a-octahydro-5-

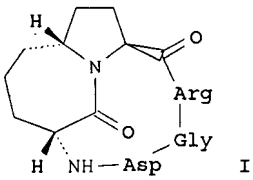
oxopyrrolo[1,2-a]azocin-3-yl]carbonyl]amino]-4,4-diethoxy-, 1,1-dimethylethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1233229 HCAPLUS
DN 144:129220
TI Targeting integrins: Insights into structure and activity of cyclic RGD pentapeptide mimics containing aza-bicyclo-alkane amino acids
AU Belvisi, Laura; Bernardi, Anna; Colombo, Matteo; Manzoni, Leonardo; Potenza, Donatella; Scolastico, Carlo; Giannini, Giuseppe; Marcellini, Marcella; Riccioni, Teresa; Castorina, Massimo; LoGiudice, Pietro; Pisano, Claudio
CS Dipartimento di Chimica Organica e Industriale and Centro Interdisciplinare Studi bio-molecolari e applicazioni Industriali, (CISI), Universita degli Studi di Milano, Milan, I-20133, Italy
SO Bioorganic & Medicinal Chemistry (2006), 14(1), 169-180
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:129220
GI



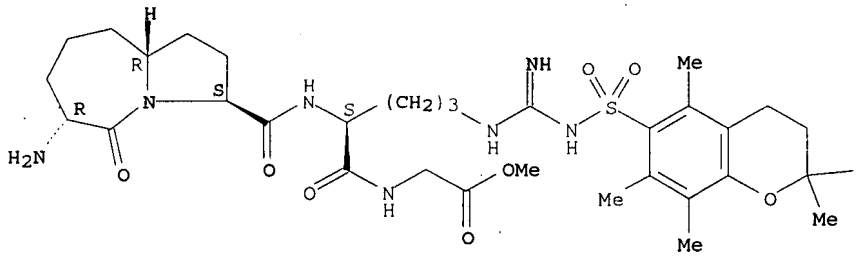
I

AB A small library of cyclic RGD pentapeptide mimics incorporating stereoisomeric 5,6- and 5,7-fused bicyclic lactams was synthesized. This library was found to contain high-affinity ligands for the αvβ3 integrin. The aim of this study was to investigate activity, selectivity, and structure of these ligands in order to identify new specific αv-integrin antagonists that could be evaluated as tumor angiogenesis inhibitors. In vitro screening, including receptor-binding assays to purified αvβ3, αvβ5, and α5β1 integrins, and platelet aggregation assay, revealed cyclo-peptide I (ST1646) as a potent, highly selective αvβ3/αvβ5 integrin antagonist. Structure determination of the cyclic RGD pentapeptide mimics performed by a combination of NMR spectroscopy, and mol. mechanics and dynamics calcns. showed a strong dependence of the RGD cyclo-peptide conformation on lactam ring size and stereochem. ST1646 revealed the highest ability within the library to adopt the proper RGD orientation required for binding to the αvβ3 integrin, as deduced from the recently solved crystal structure of the extracellular segment of integrin αvβ3 in complex with a cyclic pentapeptide ligand.
IT **873460-96-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, conformation, structure-property, of cyclic RGD pentapeptide mimics containing aza-bicyclo-alkane amino acids as integrin inhibitors)

RN 873460-96-9 HCAPLUS
CN Glycine, N2-[[(3S,6R,9aR)-6-aminooctahydro-5-oxo-1H-pyrrolo[1,2-a]azepin-3-yl]carbonyl]-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—Me

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:779650 HCAPLUS
DN 138:331199
TI Exploring relationships between mimic configuration, peptide conformation and biological activity in indolizidin-2-one amino acid analogs of gramicidin S
AU Roy, S.; Lombart, H.-G.; Lubell, W. D.; Hancock, R. E. W.; Farmer, S. W.
CS Departement de chimie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.
SO Journal of Peptide Research (2002), 60(4), 198-214
CODEN: JPERFA; ISSN: 1397-002X
PB Blackwell Munksgaard
DT Journal
LA English
OS CASREACT 138:331199
AB Indolizidin-2-one amino acids (I2aas) possessing 6S- and 6R-ring-fusion stereochem. were introduced into the antimicrobial peptide gramicidin (GS) to explore the relationships between configuration, peptide conformation and biol. activity. Solution-phase and solid-phase techniques were used to synthesize three analogs with I2aa residues in place of the D-Phe-Pro residues at the turn regions of GS: [(6S)-I2aa4-5,4'-5']GS (I), [Lys2,2',(6S)-I2aa4-5,4'-5']GS (II) and [(6R)-I2aa4-5,4'-5']GS (4). Although conformational anal. of [I2aa4-5,4'-5']GS analogs 2-4 indicated that both ring-fusion stereoisomers of I2aa gave peptides with CD and NMR spectral data characteristic of GS, the (6S)-I2aa analogs I and II exhibited more intense CD curve shapes, as well as greater nos. of nonsequential NOE between opposing Val and Leu residues, relative to the (6R)-I2aa analog, suggesting a greater propensity for the (6S)-diastereomer to adopt the β-turn/antiparallel β-pleated sheet conformation. In measurements of antibacterial and antifungal activity, the (6S)-I2aa analog I exhibited significantly better potency than the (6R)-I2aa diastereomer. Relative to GS, I exhibited usually 1/2 to 1/4 antimicrobial activity as well as 1/4 hemolytic activity. In certain cases, antimicrobial and hemolytic activities of GS were shown to be dissociated through modification at the peptide turn regions with the (6S)-I2aa diastereomer. The synthesis and evaluation of GS analogs has furnished new insight into the importance of ring-fusion stereochem. for

turn mimicry by indolizidin-2-one amino acids as well as novel antimicrobial peptides.

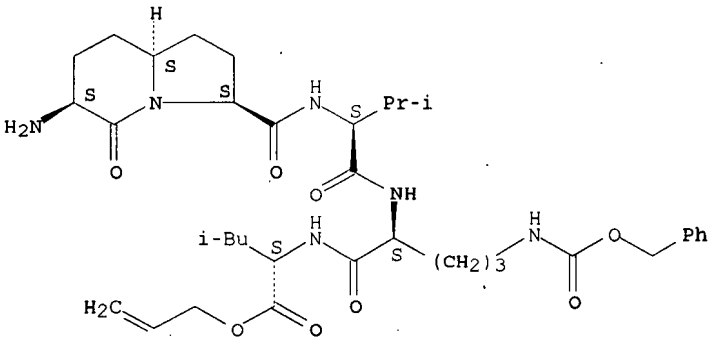
IT **518027-76-4P 518027-78-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antimicrobial structure activity relationships of indolizidin-2-one amino acid analogs of gramicidin S)

RN 518027-76-4 HCAPLUS
CN L-Leucine, N-[[(3S,6S,8aS)-6-aminooctahydro-5-oxo-3-indolizinyl]carbonyl]-L-valyl-N5-[(phenylmethoxy)carbonyl]-L-ornithyl-, 2-propenyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

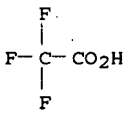
CRN 518027-75-3
CMF C36 H54 N6 O8

Absolute stereochemistry.



CM 2

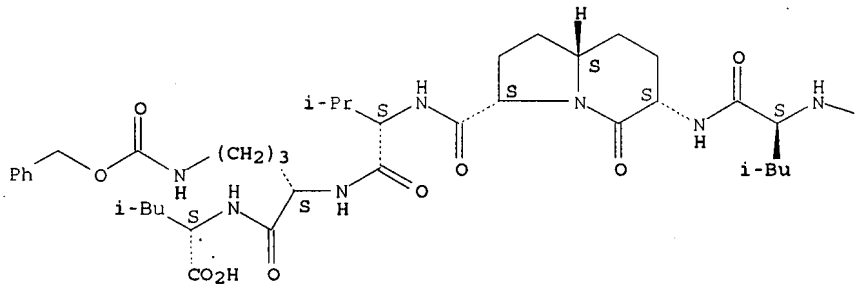
CRN 76-05-1
CMF C2 H F3 O2



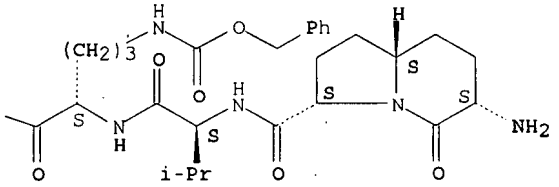
RN 518027-78-6 HCAPLUS
CN L-Leucine, N-[[(3S,6S,8aS)-6-aminooctahydro-5-oxo-3-indolizinyl]carbonyl]-L-valyl-N5-[(phenylmethoxy)carbonyl]-L-ornithyl-L-leucyl-(3S,6S,8aS)-6-aminooctahydro-5-oxo-3-indolizinecarbonyl-L-valyl-N5-[(phenylmethoxy)carbonyl]-L-ornithyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



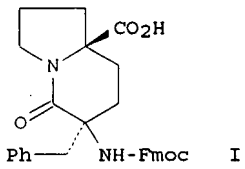
PAGE 1-B



RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitstr l37

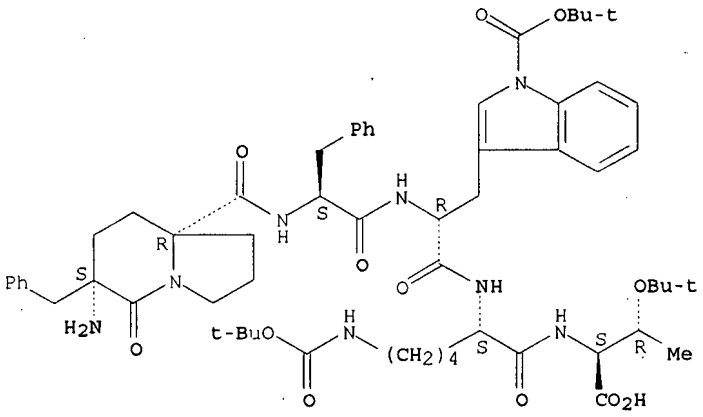
L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:858286 HCAPLUS
DN 124:56673
TI Synthesis of a type-VIβ-turn peptide mimetic and its incorporation into a high-affinity somatostatin receptor ligand
AU Gramberg, Dieter; Weber, Christoph; Beeli, Reto; Inglis, Janice; Bruns, Christian; Robinson, John A.
CS Institute Organic Chemistry, University Zuerich, Zurich, CH-8057, Switz.
SO Helvetica Chimica Acta (1995), 78(6), 1588-606
CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta
DT Journal
LA English
OS CASREACT 124:56673
GI



I

AB The synthesis of a cis-Phe-Pro dipeptide mimetic is described, which adopts a type-VIβ-turn conformation. The α-positions of Phe and Pro are joined by a CH2CH2 bridge, thereby forming a fused bicyclic system, and fixing a geometry similar to that seen in cis-Phe-Pro units in protein crystal structures. The dipeptide mimetic I was synthesized in optically pure form starting from (R)-α-allylproline, with a free carboxylic acid and an Fmoc-protected N-terminus, thereby allowing its incorporation into linear and cyclic peptides using standard solid-phase methods. The mimetic I was incorporated into the cyclic somatostatin analog cyclo(-Phe=Pro-Phe-D-Trp-Lys-Thr-), where Phe=Pro represents the mimetic. This analog shows a high affinity for somatostatin receptors. Based on NMR studies in aqueous solution, likely low-energy conformations for this analog were deduced using restrained dynamic simulated annealing. The conformations found, which include a distorted type-II' turn at D-Trp-Lys, are similar to low-energy conformations for cyclo(-Phe-Pro-Phe-D-Trp-Lys-Thr-), and to those in crystal structures of octreotide.
IT **172039-57-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of a type-VIβ-turn peptide mimetic and a high-affinity somatostatin receptor ligand containing it)
RN 172039-57-5 HCAPLUS
CN L-Threonine, N-[N2-[N-[N-[[6-aminohexahydro-5-oxo-6-(phenylmethyl)-8a(1H)-indolizinyl]carbonyl]-L-phenylalanyl]-1-[(1,1-dimethylethoxy)carbonyl]-D-tryptophyl]-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl]-O-(1,1-dimethylethyl)-, (6S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> d his

     (FILE 'HOME' ENTERED AT 09:55:20 ON 28 JUL 2007)

     FILE 'REGISTRY' ENTERED AT 09:55:31 ON 28 JUL 2007
L1             STR
L2          50 L1

     FILE 'HCAPLUS' ENTERED AT 09:58:11 ON 28 JUL 2007
L3           4 US20060217295/PN OR (US2006-549951 OR WO2004-US8108 OR US2003-4
L4           1 L3 AND NEUROPROTECTIVE

     FILE 'REGISTRY' ENTERED AT 10:00:13 ON 28 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 10:00:13 ON 28 JUL 2007
L5             TRA L4 1- RN :      107 TERMS

     FILE 'REGISTRY' ENTERED AT 10:00:13 ON 28 JUL 2007
L6         107 SEA L5
L7          12 L6 AND (NC4-NC4 OR NC4-NC5 OR NC4-NC6 OR NC4-NC7)/ES
L8         151 C16H25N3O6
L9           7 L8 AND (NC4-NC4 OR NC4-NC5 OR NC4-NC6 OR NC4-NC7)/ES
L10          6 L9 NOT ?SPIRO?

     FILE 'HCAPLUS' ENTERED AT 10:05:59 ON 28 JUL 2007
L11          2 L10
L12          4 L7
L13          4 L11-12
L14          1 L13 AND L3
L15          3 L13 NOT L14

     FILE 'REGISTRY' ENTERED AT 10:11:42 ON 28 JUL 2007
L16       1389 L1 FULL
               SAV TEM J951C16/A L16
L17            STR L1
L18         22 L17 SAM SUB=L16
L19            STR L17
L20          2 L19 SAM SUB=L16
L21         32 L19 FULL SUB=L16
               SAV TEM J951C1/A L21

     FILE 'HCAPLUS' ENTERED AT 10:16:37 ON 28 JUL 2007
L22          16 L21
               E HARRIS P/AU
L23         164 E3,E27-28
               E HARRIS PAUL/AU
L24          85 E3,E26-30
               E BRIMBLE M/AU
L25         221 E4,E6-8
L26          2 L22 AND L3,L23-25
L27          14 L22 NOT L26
               SEL HIT RN L27
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     FILE 'REGISTRY' ENTERED AT 10:19:39 ON 28 JUL 2007
L28           23 E1-23
L29            4 L28 AND (C36H54N6O8 OR C23H39N3O6 OR C66H98N12O15 OR C33H51N7O8

     FILE 'HCAPLUS' ENTERED AT 10:27:28 ON 28 JUL 2007
L30            3 L29

     FILE 'HCAOLD' ENTERED AT 10:28:21 ON 28 JUL 2007
L31            0 L21

     FILE 'REGISTRY' ENTERED AT 10:28:31 ON 28 JUL 2007
L32              STR L1
L33            1 L32 SAM SUB=L16
L34            5 L32 FULL SUB=L16
                 SAV TEM L34 J951C6/A

     FILE 'HCAPLUS' ENTERED AT 10:30:54 ON 28 JUL 2007
L35            3 L34
L36            2 L35 AND L4,L23-25
L37            1 L35 NOT L36
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 10:32:03 ON 28 JUL 2007
L38            1 E24

     FILE 'HCAOLD' ENTERED AT 10:32:25 ON 28 JUL 2007
L39            0 L34

     FILE 'HCAPLUS' ENTERED AT 10:32:51 ON 28 JUL 2007
L40            5 L15,L26,L34

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